

IN THE SPECIFICATION:

Page 21, please replace the paragraph beginning at line 8 with the following:

--In order to test whether the antibodies isolated against a gel spot had a good affinity towards the native antigen, real-time interaction analysis was performed using surface plasmon resonance on a BIAcore instrument as described (Neri et al. (1997) Nature Biotechnol., 15, 1271-1275). Monomeric fractions of E1, A2 and G4 scFv fragments bound to ED-B with affinity in the $10^7 - 10^8 \text{M}^{-1}$ range (~~Table 2~~) (Table 1).--.

Page 22, please replace the paragraph beginning at line 8, with the following:

--ScFv(E1) was selected to test the possibility of improving its affinity with a limited number of mutations of CDR residues located at the periphery of the antigen binding site (Figure 1A). We combinatorially mutated residues 31-33, 50, 52 and 54 of the antibody VH, and displayed the corresponding repertoire on filamentous phage. These residues are found to frequently contact the antigen in the known 3D-structures of antibody-antigen complexes. The resulting repertoire of 4×10^8 clones was selected for binding to the ED-B domain of fibronectin. After two rounds of panning, and screening of 96 individual clones, an antibody with 27-fold improved affinity was isolated (~~H10; Tables 1 and 2~~) (H10; Table 1). Similarly to what others have observed with affinity-matured antibodies, the improved affinity was due to slower dissociation from the antigen, rather than by improved kon values (Schier et al. (1996). Gene, 169, 147-155, Ito (1995). J. Mol. Biol., 248, 729-732). The antibody light chain is often thought to contribute less to the antigen binding affinity as supported by the fact that both natural and artificial antibodies devoid of light chain can still bind to the antigen (Ward et al. (1989) Nature, 341, 544-546, Hamers-Casterman et al. (1993). Nature, 363, 446-448). For this reason we chose to randomize only two residues (~~33~~ 32 and 50) of the VL domain, which are centrally located in the antigen binding site (Figure 1a) and often found in 3D structures to contact the antigen. The resulting library, containing 400 clones, was displayed on phage and selected for antigen binding. From

analysis of the dissociation profiles using real-time interaction analysis with a BIAcore instrument (Jonsson et al. (1991). BioTechniques, 11, 620-627) and koff measurements by competition experiments with electrochemiluminescent detection a clone (L19) was identified, that bound to the ED-B domain of fibronectin with a $K_d=54$ pM Table 1.